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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/775,409	02/10/2004	Bruce A. Beutel	7285.US.01	1598
23492	7590	10/25/2006		
ROBERT DEBERARDINE ABBOTT LABORATORIES 100 ABBOTT PARK ROAD DEPT. 377/AP6A ABBOTT PARK, IL 60064-6008			EXAMINER JOIKE, MICHELE K	
			ART UNIT 1636	PAPER NUMBER
DATE MAILED: 10/25/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/775,409	Applicant(s) BEUTEL ET AL.	
	Examiner Michele K. Joike, Ph.D.	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 September 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) 6 and 16-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-15 and 25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 February 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>02/10/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I in the reply filed on September 1, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 6 and 16-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 1, 2006. Claims 1-5, 7-15 and 25 are examined.

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claim 8 contains a range of 10 to 50 for the panel of restriction enzymes. This range is not found in the specification.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Page 15 contains the hyperlink.

Claim Objections

Claim 7 is objected to because of the following informalities: There should be an "of" after "panel" and before "restriction" in line 1. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 10, upon which claim 11 is dependent, disclose a single phenotype that is to be observed, but claim 11 appears to combine three different phenotypes to be observed. It is unclear whether all three phenotypes need to be present.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 10-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Tomb et al.

Applicants claim a method of identifying the location of a mutation in the genome of a bacteria comprising isolating the DNA, digesting it, transforming the fragments into a non-mutated host organism to transform it into a mutated host organism, determining the transformation frequency and correlating it to provide information about the location of the mutation. The bacteria has had its entire genome determined. The mutated phenotype is drug resistance (resistance to antibacterial agents) or increased production of secondary metabolites.

Tomb et al (J. Bac. 171(7): 3796-3802, 1989, specifically Abstract, pp. 3796 and 3798) teach Pst1 digested DNA fragments transformed into *Haemophilus influenzae*. The DNA was mutated before the transformation, then transformation frequency was measured. Mutation phenotypes included transformation inefficiency and kanamycin resistance. Restriction mapping was performed to identify where the mutated DNA fragments inserted into the chromosome. *H. influenzae* has had its entire genome determined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 7, 14, 15 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tomb et al in view of Smith et al.

Applicants teach a panel of restriction enzymes used to digest the DNA including *Dra1*, *Ase1* and *Ssp1*. There is also a restriction map printout obtained by a computer.

Tomb et al (J. Bac. 171(7): 3796-3802, 1989, specifically Abstract, pp. 3796 and 3798) teach all of the limitations as described above. However, Tomb et al do not teach using a panel of restriction enzymes used to digest the DNA or a restriction map printout obtained by a computer.

Smith et al (J. Bac. 172(3): 1167-1172, 1990, specifically Table 1, pp. 1170 and 1171) teach using *Dra1*, *Ase1* and *Ssp1* for restriction mapping. They further teach using computational methods for producing high-resolution restriction maps.

The ordinary skilled artisan, desiring to use a panel of restriction enzymes used to digest the DNA and a restriction map printout obtained by a computer, would have been motivated to combine the teachings of Tomb et al on a method for transforming mutated, digested DNA fragments into *H. influenzae* and then performing a restriction map with Smith et al on using *Dra1*, *Ase1* and *Ssp1* and a computer for restriction

mapping because Smith et al teach when mapping a new genome, the size of a genome is not known, so using a variety of enzymes will allow for smaller fragments which give finer tuned maps. It would have been obvious to one of ordinary skill in the art to use computational methods because Smith et al state that automatic sequencing devices allow for faster analysis and sequencing of more massive amounts of DNA. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tomb et al in view of Ivanova et al.

Applicant teaches using a partially sequenced bacterial genome in the above method.

Tomb et al (J. Bac. 171(7): 3796-3802, 1989, specifically Abstract, pp. 3796 and 3798) teach all of the limitations as described above. However, Tomb et al do not teach using partially sequenced bacteria.

Ivanova et al (Nature 423: 87-91, 2003, specifically pp. 87 and 90) teach genomic sequencing of *Bacillus cereus* by fractionating DNA.

The ordinary skilled artisan, desiring to sequence a partially sequenced genome, would have been motivated to combine the teachings of Tomb et al on a method for transforming mutated, digested DNA fragments into *H. influenzae* and then performing a restriction map with Ivanova et al teaching genomic sequencing of *Bacillus cereus*

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because Ivanova et al teach that sequencing a genome enables comparative analysis with other genomes of biological significance, like *Bacillus anthracis*, to identify conserved genes. Also, one would have been motivated to choose *Bacillus cereus* because it is an opportunistic food pathogen causing food poisoning. It would have been obvious to one of ordinary skill in the art to use the partially sequenced *B. cereus* because Ivanova et al teach that a complete genome sequence provides a basis for phylogenetic analysis and ability to explore genetic diversity. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Although only *Bacillus cereus* was described in the Ivanova et al reference, the same rationale above applies to all of the partially sequenced genomes listed in claim 5.

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tomb et al in view of Kent et al.

Applicants teach use of restriction enzymes comprising 10 to 50 restriction enzymes.

Tomb et al (J. Bac. 171(7): 3796-3802, 1989, specifically Abstract, pp. 3796 and 3798) teach all of the limitations as described above. However, Tomb et al do not teach using multiple restriction enzymes.

Kent et al (Appl. Environ. Microbiol, 69(11): 6768-6776, 2003, specifically 6768, 6769, 6770 and 6774) teach using computational analysis and RFLP to analyze profiles of microbial communities. They also teach the use of 27 restriction enzymes.

The ordinary skilled artisan, desiring to sequence a partially sequenced genome, would have been motivated to combine the teachings of Tomb et al on a method for transforming mutated, digested DNA fragments into *H. influenzae* and then performing a restriction map with Kent et al on using 27 restriction enzymes to create a RFLP profile because Kent et al teach that the use of multiple digests is recommended to accomplish any degree of phylogenetic resolution. It would have been obvious to one of ordinary skill in the art to use multiple digests because Kent et al teach that use of a single digest diminishes predictive power because of inaccuracies in fragment size measurements. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tomb et al in view of US 6,207,442.

Applicants teach transformation by electroporation.

Tomb et al (J. Bac. 171(7): 3796-3802, 1989, specifically Abstract, pp. 3796 and 3798) teach all of the limitations as described above. However, Tomb et al do not teach transformation by electroporation.

US 6,207,442 (specifically columns 5 and 11) teach transforming fragments of DNA by electroporation.

The ordinary skilled artisan, desiring to sequence a partially sequenced genome, would have been motivated to combine the teachings of Tomb et al on a method for transforming mutated, digested DNA fragments into *H. influenzae* and then performing a restriction map with US 6,207,442 on electroporation transformation because US 6,207,442 teach that linear DNA fragments cannot replicate and must be integrated into the chromosome. It would have been obvious to one of ordinary skill in the art to use eletroporation because US 6,207,442 teach that it is a widely used method for transforming exogenous DNA into host cells. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele K. Joike, Ph.D. whose telephone number is 571-272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michele K Joike, Ph.D.
Examiner
Art Unit 1636


DAVID GUZO
PRIMARY EXAMINER